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2nd MEETING OF SCIENTIFIC RESEARCH GROUP  
MONTREAL AUGUST 6th-8th 1986

Present: Dr. R.E. Thornton  
Dr. S.R. Massey  
Dr. M. Bilimoria  
Mr. R.G. Nicholls  
Dr. G. Smith  
Dr. F. Knabjohann  
Dr. F. Seehofer  
Dr. J.G. Esterle  
Dr. G. Gori  
Dr. W. Templeton

BAT Co. London  
] Imperial Tobacco Ltd., Montreal  
W.D. & H.O. Wills, Sydney  
] BAT UKE, Southampton  
] BAT Cigaretten Fabriken, Hamburg  
Brown & Williamson, Louisville, Kentucky  
] Consultants

Nicotine

Dr. Gori discussed the results of a behavioural study of 799 subjects carried out in the U.S.A., strongly pointing to nicotine as the basis of the smoking habit. For example plasma nicotine levels were almost constant, regardless of measured machine smoked delivery levels, as were the number of cigarettes smoked per day. Dr. Gori went on to discuss the possibilities for products in the future including changes in Tar/Nicotine ratios and nicotine aerosols. Dr. Gori said that further work to demonstrate that some of the effects of smoking were due to nicotine was still required.

In a broad look at nicotine toxicology, covering carcinogenicity, promoting activity, mutagenicity and a possible rôle in cardiovascular disease Dr. Gori considered the evidence that nicotine had activity to be equivocal at best and frequently weak or non-existent. Some good studies also existed in which no activity was seen (e.g. carcinogenicity). However he suggested that a repetition of a well planned study looking at carcinogenicity might be justified. Dr. Gori also commented on the multifactorial nature of cardiovascular disease.

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Dr. Gori considered that work in relation to diseases negatively associated with smoking might be justified, e.g. colon cancer, Alzheimer's disease etc.

Finally in regard to the allegation that nicotine was addictive, Dr. Gori said that this was a problem in semantics and pointed out that the reinforcing effects of smoking (and presumably nicotine) were entirely positive.

Dr. Templeton described the distribution of receptors for acetylcholine and the current status of work using materials such as  $\alpha$ -bungarotoxin to probe for binding sites. It was now realized that  $\alpha$ -bungarotoxin did not necessarily bind at the same sites as nicotine; implying, perhaps, that an endogenous ligand exists for such sites. However, since there is some binding of nicotine at "bungarotoxin" sites the possibility exists that the effects of nicotine might be enhanced by effects at the adjacent "bungarotoxin" receptors.

Studies of receptor sites using modern techniques of molecular biology were described. Brain acetylcholine receptors have been shown to possess 4 cysteine units at similar places. With regard to the human diseases (Parkinsons and Alzheimer's disease) it was pointed out that patients presenting were at an advanced stage of degeneration because the brain functioned even with 70% or so of neurons out of action.

With regard to the effects of smoking on cognitive performance more work was needed to clarify the research of Warburton which was rather isolated, particularly concentrating on nicotine and on whether it caused an intrinsic increase in performance.

Experiments in non-human primates did not support the view that smoking was addictive. Training non-human primates to smoke required a reward and water (a basic necessity of life) had to be used, and after removal of the reward the % of 'smokers' was as low as 2%. Attempts to classify materials such as nicotine, amphetamine, caffeine, heroin etc. showed that each material was unique.

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